

## **REMARKS**

Claims 1-10, 25, 28, and 30-38 are cancelled. Claims 11, 13, 15-17 and 50 are amended. New claims 59-60 are added. Claims 11-24, 26, 27, 29, 44-58 and 59-60 are pending.

### **I. Objection to Specification**

The specification was objected to as failing to provide proper antecedent basis for the claimed subject matter of claim 13. Applicant amended claim 13 to reflect that an “erodible matrix” refers to an “erodible elastomeric matrix.” Applicants believe that the amendment is properly supported by the specification.

### **II. Claim Rejections Under 35 USC § 112, First Paragraph**

The Examiner rejected claims 11-24, 26-27 and 44-58 under 35 U.S.C. 112, first paragraph, stating that while the specification is “enabling for the treatment of certain disease using a particular 2'-deoxynucleoside analog, [it] does not reasonably provide enablement for treating all types of diseases using any 2'-deoxynucleoside analog.” See Office Action, p.5.

In light of the present Amendment, Applicant respectfully traverses Examiner’s rejection of claims 11-24, 26-27 and 44-58 under 35 U.S.C. 112, first paragraph. Independent claim 11, as currently amended, specifies a method for treating a disease in a patient, wherein the disease is selected from the following diseases: a hematological malignancy, solid tumor, ischemia, autoimmune disease, inflammatory disease, stroke, myocardial infarction, and ventricular arrhythmia. The language supporting this amendment appears in the specification at page 8, lines 16-27, and at page 29, lines 13-22.

The Examiner also rejected claims 48 and 58 under 35 U.S.C. 112, first paragraph, based on lack of enablement. According to the Examiner, “while being enabling for the reduction of acid concentration in the stomach using an antacid, such as calcium carbonate, or a histamine H2 inhibitor, such as cimetidine, [the specification] does not reasonably provide enablement for the reduction of acid concentration in the stomach using a proton pump inhibitor.” See Office Action p. 6.

Applicant respectfully transverses Examiner’s rejection of claims 48 and 58 under 35 U.S.C. 112, first paragraph for the following reason. Proton pump inhibitors have been well known to the skilled ones in the relevant field since at least 1988. See <http://www.cfhp.com/DocumentLibrary/DocFiles/21-PHProtonPump.pdf>, a copy of which

is submitted herewith as "Exhibit A". A "proton pump inhibitor" is a commonly used term of art which refers simply to a class of compounds that inhibits gastric acid by blocking the hydrogen-potassium adenosine triphosphatase enzyme system. See [http://bnf.vhn.net/bnf/documents/bnf.248.html#BNFID\\_2137](http://bnf.vhn.net/bnf/documents/bnf.248.html#BNFID_2137), a copy of which is submitted herewith as "Exhibit B". Currently there are about five commonly used members of the "proton pump inhibitor" class of compounds on the market. See [http://www.bupa.co.uk/health\\_information/html/medicine/proton\\_pump.html#4](http://www.bupa.co.uk/health_information/html/medicine/proton_pump.html#4), a copy of which is submitted herewith as "Exhibit C". These proton pump inhibitors are: omeprazole, esomeprazole, lansoprazole, pantoprazole and rabeprazole. As this class of compounds is limited in number and as it is well known in the art, one of ordinary skill in the art would understand how to make and use these proton pump inhibitors for treating the particular diseases specified in claim 11 and 50. Dependent claims 48 and 58 are enabled under 35 U.S.C. 112, first paragraph.

For the foregoing reasons, Applicant respectfully requests that the Examiner withdraw the rejection under 35 U.S.C. §112, first paragraph.

### **III. Claim Rejections - 35 USC § 112, Second Paragraph**

The Examiner rejected claims 11-24, 26-27, 29 and 44-58 under 35 U.S.C. 112, second paragraph, as being indefinite as to the following terms and phrases: "2'-deoxyadenosine analog," "treating a patient," and "proton pump inhibitor."

Applicant respectfully traverses Examiner's rejection under 35 U.S.C. 112, second paragraph for the following reasons.

First, the term "2'-deoxyadenosine analog" in claims 11, 13-24, 26-27, 29, 44-52 and 54-58 is not indefinite. The term "adenosine" is well known in the art, and as its name suggests, refers to ribonucleotide which consists of the nitrogenous base adenine linked to the sugar ribose. In addition, the term "adenosine analogs" has been defined by the present invention as modifications of adenosine such as, "2'-deoxycoformycin (also referred to as dCF, pentostatin, or NIPENT®), an inhibitor of adenosine deaminase; fludarabine monophosphate (FLU), a fluorinated analogue of adenine that is relatively resistant to adenosine-deaminase and 2-chloro-2'-deoxyadenosine (also known as cladribine or 2CDA) a drug also resistant to adenosine deaminase through introduction of a chlorine at the 2 carbon. Other adenosine analogs that have useful activity include deoxyadenosines generally, including 2'deoxyadenosine, 3'-deoxyadenosine, and dideoxyadenosine." See Specification, page 1. The term "2'-deoxyadenosine analog" merely refers to those "adenosine analogs" which have a 2'-deoxy or an

elimination of a 2'-hydroxy group from the ribose ring. Thus, the term is sufficiently definite to one of ordinary skill in the art and is limited by the above metes and bounds.

Second, the phrase "treating a patient" in claims 11-20, 24, 26-27, 29 and 44-58, is also sufficiently definite in view of the amendments to independent claims 11 and 50. As the above amendments include a specific group of particular diseases for which a patient is being treated, Applicants submit that the term "treating a patient" is understood by a person skilled in the art to mean treating a patient having a disease from this specifically defined group of diseases.

Third, the phrase "proton pump inhibitor" in claims 48 and 58 is also sufficiently definite. As discussed above, the class of compounds that would be considered a "proton pump inhibitor" of this invention is those compounds which inhibit gastric acid by blocking the hydrogen-potassium adenosine triphosphatase enzyme system (e.g., omeprazole, esomeprazole, lansoprazole, pantoprazole and rabeprazole). As this is a well-defined class of compounds, which is well known in the art, the phrase "proton pump inhibitor" in claims 48 and 58 is not indefinite.

For the foregoing reasons, Applicants respectfully request that the Examiner withdraw the rejection under 35 U.S.C. §112, second paragraph.

#### **IV. Claim Rejections Under 35 USC § 102(b)**

##### **1. Rejection in view of BMS**

The Examiner rejected claims 11, 16, 20, 46-47, 50-52 and 56-57 under 35 U.S.C. §102(b) as being anticipated by EP 0 524 579 to BMS (hereinafter referred to as "BMS").

The Examiner states that BMS teaches a formulation of dideoxy purine nucleotides incorporating a reduced acid buffer. See page 2, lines 9-25. However, nowhere in BMS reference is there any teaching or suggestion of using a 2'-deoxyadenosine analog for the treatment of a disease selected from a group specified in claims 11 and 50: hematological malignancy, solid tumor, ischemia, autoimmune disease, inflammatory disease, stroke, myocardial infarction, and ventricular arrhythmia. BMS merely teaches using some adenosine analogs such as ddA and ddI for the treatment of viral infection such as HIV infection. See page 1, lines 39-42; and page 9, lines 29-32. Therefore BMS fails to anticipate the claims invention as it does not describe all of the limitations of the presently claimed invention. Thus, Applicants respectfully request that the Examiner withdraw the above rejection under 35 U.S.C. §102(b).

2. Rejection in view of Schinazi

The Examiner also rejected claims 11, 14, 16-17, 20, 24, 46, 49-50, 52 and 56 under 35 U.S.C. 102(b) as being anticipated by U.S. Patents Nos. 5,118,672 ('672) and 5,159,067 ('067) both to Schinazi.

Both '672 and '067 independently disclose compounds 2',3'-dideoxyadenosine, 2',3'-dideoxy-N<sup>6</sup>-methyladenosine and their diphosphohexose derivatives for use in the treatment of HIV. *See* '672, Column 30, line 66 to Column 31, line 8; *see also* '067, Column 13, lines 52-62. However, neither '672 nor '067 discloses the use of the above compounds, with or without additional the additional acid protecting compounds, for the treatment of diseases selected from the group consisting of hematological malignancy, solid tumor, ischemia, autoimmune disease, inflammatory disease, stroke, myocardial infarction, and ventricular arrhythmia, as defined in claims 11 and 50. Therefore these two cited references fail to anticipate the claimed invention as they do not describe all of the limitations of the presently claimed invention.

For the foregoing reasons, applicants respectfully request that the Examiner withdraw the rejection under 35 U.S.C. §102(b).

**V. Claim Rejections Under 35 USC § 103(a)**

The Examiner rejected the pending claims in view of several different combinations of references under 35 U.S.C. §103(a). As will be discussed in detail below, none of the combinations of cited references teaches or suggests one of ordinary skill in the art to modify the teaching of the cited references and arrive at the claimed invention having all of the limitations specified in independent claims 11 and 50.

In order to establish a *prima facie* case of obviousness, all of the claimed limitations must be taught or suggested by the prior art. See MPEP 2143.03. "If the examiner does not produce a *prima facie* case, the applicant is under no obligation to submit evidence of nonobviousness." MPEP 2142. Applicants submit that a *prima facie* case of obviousness has not been established for the following reasons.

1. Rejection over BMS in view of Carson and Gallagher

The Examiner rejected claims 11-24, 26-27, 29, 46-47, 49-53 and 56-57 as being unpatentable under 35 U.S.C. §103(a) over BMS in view of U.S. patent No. 5,310,732 ("Carson") and U.S. Pat. No. 5,366,960 ("Gallagher").

As discussed above in response to the Examiner's rejection under 35 U.S.C. §102(b), BMS teaches the use of 2',3'-dideoxypurine nucleosides, such as 2',3'-dideoxyadenosine (ddA), 2',3'-dideoxyinosine (ddI) and 2',3'-dideoxyguanosine (ddG) and their triphosphates in combination with a compound that reduces acidity in the gastrointestinal tract for the treatment of HIV. Thus, BMS fails to teach the claimed method for treating the particular disease specified in claims 11 and 50.

On the other hand, Carson *et al.* teaches the use of 2'-halo-2'-deoxyadenosine compounds, in particular 2'-chloro-2'-deoxyadenosine, for the treatment of various monocyte-mediated disorders, such as rheumatoid arthritis and multiple sclerosis. As acknowledged by the Examiner, Carson *et al.* discloses using **liposomal** formulation such as phosphatidyl cholines or using **enteric** formulation that serve as a physical barrier to protect 2'-halo-2'-deoxyadenosine from disintegration in the acidic environment by preventing the drug from being exposed to the acid too early. However, nowhere in Carson *et al.* is there a teaching or suggestion of the claimed method of orally administering a 2'-deoxyadenosine analog in combination with an agent that actually **reduces acid concentration** in the stomach as oppose to inhibiting the acid from reaching the 2'-deoxyadenosine analog.

The third reference Gallagher fails to motivate one of ordinary skill in the art to modify BMS and Carson *et al.* to arrive at the claimed invention. As acknowledged by the Examiner, Gallagher merely teaches formulating pentostatin by using magnesium carbonate, methycellulose, sodium carboxymethylcellulose and the like. Thus Gallagher fails to teach the claimed method of oral administering a 2'-deoxyadenosine analog in combination with an agent that **reduces acid concentration** in the stomach so that the chemical decomposition of the drug could be inhibited.

As none of the references above, independently or in combination, teach or suggest the use of a 2'-deoxyadenosine analog and an anti-acid agent for treating a hematological malignancy, solid tumor, ischemia, autoimmune disease, inflammatory disease, stroke, myocardial infarction, and ventricular arrhythmia, a *prima facie* case of obviousness has not been established. Applicants respectfully request that the Examiner withdraw this rejection under 35 U.S.C. §103(a).

## 2. Rejection over BMS in view of the Merck Index

The Examiner further rejected claims 11, 16, 20, 44-48, 50-52 and 54-58 under 35 U.S.C. §103(a) as being unpatentable over BMS in view of "The Merck Index," Twelfth Edition, 1996, 2337.

As discussed above, BMS teaches the use of 2',3'-dideoxypurine nucleosides, such as ddA, ddI, ddG and their triphosphates in combination with a compound that reduces acidity in the gastrointestinal tract for the treatment of HIV. On the other hand, the Merck Index teaches that cimetidine is a “[c]ompetitive histamine H<sub>2</sub>-receptor antagonist which inhibits gastric acid secretion and reduces pepsin output.” *See Merck*, p. 2343. As neither of these two references, independently or in combination, teaches or suggests the use of 2-deoxyadenosine analogs for treating a hematological malignancy, solid tumor, ischemia, autoimmune disease, inflammatory disease, stroke, myocardial infarction, and ventricular arrhythmia, a *prima facie* case of obviousness has not been established. Applicants respectfully request that the Examiner withdraw this rejection 35 U.S.C. §103(a).

### 3. Rejection over Schinazi in view of Itoh

The Examiner also rejected claims 11, 13-20, 24, 26-27, 29, 46-47, 49-50, 52 and 56-57 under 35 U.S.C. §103(a) as being unpatentable over U.S. Pat. Nos. 5,118,672 ('672) and 5,159,067 ('067) (collectively “Schinazi”) in view of U.S. Pat. No. 5,194,464 to Itoh *et al.* (Itoh).

As discussed above in response to the Examiner’s rejection under 35 U.S.C. §102(b), both patents to Schinazi teach that compounds, such as 2',3'-dideoxyadenosine and 2',3'-dideoxy-N<sup>6</sup>methyladenosine and their diphosphohexose derivatives are useful in treating viral infections like HIV.

On the other hand, as acknowledged by the Examiner, “Itoh discloses enteric films that excel in film strength and acid resistance for use in pharmaceutical preparations.” Office Action, p. 16. As neither Schinazi nor Itoh, independently or in combination, teaches or suggests the use of a 2-deoxyadenosine analog in combination with an anti-acid agent for treating a hematological malignancy, solid tumor, ischemia, autoimmune disease, inflammatory disease, stroke, myocardial infarction, and ventricular arrhythmia, a *prima facie* case of obviousness has not been established. Applicants respectfully request that the Examiner withdraw this rejection 35 U.S.C. §103(a).

### 4. Rejection over Schinazi in view of Shimuzu

Fourth, the Examiner rejected claims 11, 13-20, 24, 26-27, 29, 46-47, 49-50, 52 and 56-57 under 35 U.S.C. 103(a) as being unpatentable over Schinazi in view of U.S. Pat. No. 5,824,339 to Shimuzu *et al.* (Shimuzu).

As discussed above in response to the Examiner’s rejection under 35 U.S.C. §102(b), both patents to Schinazi teach that compounds, such as 2',3'-dideoxyadenosine and 2',3'-

dideoxy-N<sup>6</sup>methyladenosine and their diphosphohexose derivatives are useful in treating viral infections like HIV.

On the other hand, as stated by the Examiner, "Shimizu teaches effervescent compositions comprising a physiologically active substance, an enteric coating, an effervescent component and an auxiliary effervescent agent that provides for the controlled release of the physiologically active substance." Office Action, p. 18. Shimizu further discloses that the physiologically active substance can be adenosine triphosphate and that the formulations can include calcium carbonate additive. *See* Shimizu, Column 5, lines 32-33.

As neither Schinaz nor Shimizu, independently or in combination, teaches or suggests the use of a 2-deoxyadenosine analog in combination with an anti-acid agent for treating a hematological malignancy, solid tumor, ischemia, autoimmune disease, inflammatory disease, stroke, myocardial infarction, and ventricular arrhythmia, a *prima facie* case of obviousness has not been established. Applicants respectfully request that the Examiner withdraw this rejection 35 U.S.C. §103(a).

##### 5. Rejection over Shinazi in view of Fuisz

The Examiner also rejected claims 11, 13-20, 24, 26-27, 29, 46, 49-50, 52 and 56 under 35 U.S.C. §103(a) as being unpatentable over 'Schinazi in view of U.S. Pat. No. 5,518,730 to Fuisz (Fuisz).

As discussed above in response to the Examiner's rejection under 35 U.S.C. §102(b), both patents to Schinazi teach that compounds, such as 2',3'-dideoxyadenosine and 2',3'-dideoxy-N<sup>6</sup>methyladenosine and their diphosphohexose derivatives are useful in treating viral infections like HIV.

On the other hand, as stated by the Examiner, "Fuisz teaches controlled release delivery systems using melt spun biodegradable polymers as carriers for bio-effecting agents." See Office Action, p. 24.

As neither Schinaz nor Fuisz, independently or in combination, teaches or suggests the use of a 2-deoxyadenosine analog in combination with an anti-acid agent for treating a hematological malignancy, solid tumor, ischemia, autoimmune disease, inflammatory disease, stroke, myocardial infarction, and ventricular arrhythmia, a *prima facie* case of obviousness has not been established. Applicants respectfully request that the Examiner withdraw this rejection 35 U.S.C. §103(a).

**CONCLUSION**

In light of the amendments and remarks set forth above, Applicants respectfully solicit the Examiner to expedite prosecution of this patent application to issuance. Should the Examiner have any questions, the Examiner is encouraged to telephone the undersigned

Respectfully submitted,  
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## Proton Pump Inhibitor Guidelines

Proton pump inhibitors (Omeprazole, Lansoprazole) became available in 1988 as a new class of antisecretory agents. They are extremely potent. Initially, extended administration of the agents was contraindicated because of the occurrence of hyperplasia and gastrointestinal malignancies in experimental animals. Use was restricted to an 8-week period recommended for ulcer healing. Once the ulcer has healed, maintenance therapy with an H2 blocker should be instituted.

Although the manufacturers still advise to avoid long-term use of these agents, prescribers have fallen into an extended pattern of use because of a favorable patient response and patient demand. A significant portion of current proton pump inhibitor (PPI) use is for non-ulcerative dyspepsia or vague abdominal pain. The use of PPIs for these indications is discouraged and unnecessary.

The purpose of the guidelines is to ensure that all members of Community First who are being prescribed PPIs receive accepted standards of care. These guidelines will promote consistency in clinical practice and improve the quality and outcome of care for our members.

### Indications:

Omeprazole and lansoprazole are approved by the FDA for the short-term (< 4 week) treatment of duodenal ulcer, short-term (< 8 week) and maintenance treatment for healing and symptomatic relief of erosive esophagitis, and for Zollinger-Ellison syndrome.<sup>1</sup> Studies have shown the proton pump inhibitors to be effective for the prevention of recurrent peptic ulcer disease, treatment of gastric ulcers, peptic ulcers refractory to H2-receptor antagonists, eradication of Helicobacter pylori, ulcers caused by nonsteroidal antiinflammatory agents, and the treatment of Barrett's esophagus.

### Dosage: Adult

#### Comparative Adult Dosages of Proton Pump Inhibitors <sup>1,2</sup>

	Duodenal Ulcer	Erosive Esophagitis	Pathological Hypersecretory Conditions
Lansoprazole (Prevacid®)	15 mg/day Duration = 4 wks	30 mg/day Duration = 8 wks However, may repeat for 8 wks	Initially, 60 mg/day and titrate to patient response
Omeprazole (Prilosec®)	20 mg/day Duration = 4-8 wks	20-40 mg/day Duration = 4-8 wks However, may repeat for 4 wks	Initially, 60 mg/day and titrate to patient response

### Pediatric

The safety and efficacy of lansoprazole and omeprazole in children have not been established.<sup>1,2</sup> Omeprazole at a starting dose of 0.7 mg/kg once daily is recommended with a range of effective dosages of 0.7-3.3 mg/kg/day.<sup>3</sup>

### References

1. Product information. Prevacid(r) (lansoprazole). Deerfield, IL: TAP Pharmaceuticals Inc., February, 1996.
2. Product Information. Prilosec(r) (omeprazole). West Point, PA: Merck and Company, Inc., April, 1996.
3. J Pediatr 1993;23:148-54.

**BNF No. 44 (September 2002)**

- General information and late changes**
- Guidance on prescribing**
- Emergency treatment of poisoning**
- 1: Gastro-intestinal system**
  - 1.1 Dyspepsia and gastro-oesophageal reflux disease**
  - 1.2 Antispasmodics and other drugs altering gut motility**
  - 1.3 Ulcer-healing drugs**
    - Helicobacter pylori infection**
    - NSAID-associated ulcers**
    - 1.3.1 H2-receptor antagonists**
    - 1.3.2 Selective antimuscarinics**
    - 1.3.3 Chelates and complexes**
    - 1.3.4 Prostaglandin analogues**
    - 1.3.5 Proton pump inhibitors**
      - OMEPRAZOLE**
      - ESOMEPRAZOLE**
      - LANSOPRAZOLE**
      - PANTOPRAZOLE**
      - RABEPRAZOLE SODIUM**
      - 1.3.6 Other ulcer-healing drugs**
        - 1.4 Acute diarrhoea**
        - 1.5 Chronic bowel disorders**
        - 1.6 Laxatives**
        - 1.7 Local preparations for anal and rectal disorders**
        - 1.8 Stoma care**
        - 1.9 Drugs affecting intestinal secretions**
    - 2: Cardiovascular system**
    - 3: Respiratory system**
    - 4: Central nervous system**
    - 5: Infections**
    - 6: Endocrine system**
    - 7: Obstetrics, gynaecology, and urinary-tract disorders**
    - 8: Malignant disease and immunosuppression**
    - 9: Nutrition and blood**
    - 10: Musculoskeletal and joint diseases**
    - 11: Eye**
    - 12: Ear, nose, and oropharynx**
    - 13: Skin**
    - 14: Immunological products and vaccines**
    - 15: Anaesthesia**
    - Appendix 1: Interactions**
    - Appendix 2: Liver Disease**
    - Appendix 3: Renal Impairment**
    - Appendix 4: Pregnancy**
    - Appendix 5: Breast-feeding**
    - Appendix 6: Intravenous Additives**

**1.3.5 Proton pump inhibitors**

The proton pump inhibitors **omeprazole**, **esomeprazole**, **lansoprazole**, **pantoprazole** and **rabeprazole** inhibit gastric acid by blocking the hydrogen-potassium adenosine triphosphatase enzyme system (the 'proton pump') of the gastric parietal cell. Proton pump inhibitors are effective short-term treatments for *gastric and duodenal ulcers*; they are also used in combination with antibacterials for the eradication of *Helicobacter pylori* (see *Helicobacter pylori infection*, **Section 1.3**). An initial short course of a proton pump inhibitor is the treatment of choice in *gastro-oesophageal reflux disease* with severe symptoms; patients with endoscopically confirmed *erosive, ulcerative, or stricturing oesophagitis* usually need to be maintained on a proton pump inhibitor (**section 1.1**).

Proton pump inhibitors are also used in the prevention and treatment of *NSAID-associated ulcers* (see **NSAID-associated ulcers** and guidance issued by NICE, below). In patients who need to continue *NSAID* treatment after an ulcer has healed, the dose of proton pump inhibitor should normally not be reduced because asymptomatic ulcer deterioration may occur.

*Omeprazole* is effective in the treatment of the *Zollinger-Ellison syndrome* (including cases resistant to other treatment); *lansoprazole* is also indicated for this condition.

**CAUTIONS.** Proton pump inhibitors should be used with caution in patients with liver disease (Appendix 2), in pregnancy (Appendix 4) and in breast-feeding. Proton pump inhibitors may mask symptoms of gastric cancer; particular care is required in those whose symptoms change and in those over 45 years of age; the presence of gastric malignancy should be excluded before treatment.

**SIDE-EFFECTS.** Side-effects of the proton pump inhibitors include gastro-intestinal disturbances (including diarrhoea, nausea and vomiting, constipation, flatulence, abdominal pain), headache, hypersensitivity reactions (including rash, urticaria, angioedema, bronchospasm, anaphylaxis), pruritus, dizziness, peripheral oedema, muscle and joint pain, malaise, blurred vision, depression and dry mouth. Proton pump inhibitors decrease gastric acidity and may increase the risk of gastro-intestinal infections.

**NICE advic (proton pump inhibitors)**

NICE has provided guidance on the use of proton pump inhibitors for the following indications:

- *Gastro-oesophageal reflux disease*—use only for severe

-  [Appendix 7: Borderline substances](#)
-  [Appendix 8: Wound management products and elastic hosiery](#)
-  [Appendix 9: Cautionary and advisory labels for dispensed medicines](#)
-  [Dental Practitioners' Formulary](#)
-  [Nurse Prescribers' Formulary](#)

symptoms (reduce dose when symptoms abate) and in disease complicated by stricture, ulceration, or haemorrhage (full dose should be maintained);

- NSAID-associated ulceration in patients who need to continue NSAID treatment—on healing of the ulcer a lower dose of proton pump inhibitor may be used [but see notes above].

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## Proton pump inhibitors

In a previous medicine of the week, we looked at H<sub>2</sub> antagonists, such as ranitidine. Here we look at the other main family of drugs used to treat stomach ulcers. The most well known proton pump inhibitor is omeprazole (Losec).

[How do proton pump inhibitors work?](#)

[What are they for?](#)

[Side effects](#)

[Use proton pump inhibitors with care if ...](#)

[Interactions with other medicines](#)

[How to use a proton pump inhibitor](#)

[Common proton pump inhibitors](#)

[Self-help for ulcers](#)

### How do proton pump inhibitors work?

Your stomach produces acid to help break down food so it is easier to digest. In certain circumstances, this acid can irritate the lining of your stomach and duodenum (the top end of your small intestine), causing indigestion and even ulceration and bleeding. The proton pump inhibitors work by completely blocking the production of stomach acid. They do this by inhibiting (shutting down) a system in the stomach known as the proton pump. The full name for this system is 'hydrogen-potassium adenosine triphosphate enzyme system'.



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### What are they for?

Proton pump inhibitors are used to heal stomach and duodenal ulcers. This includes stomach ulcers caused by taking nonsteroidal anti-inflammatory drugs. They are also used to relieve symptoms of oesophagitis (inflammation of the oesophagus or gullet) and severe gastro-oesophageal reflux, a condition where acid leaks up from the stomach into the gullet.

In combination with certain antibiotics (e.g. amoxycillin and

clarithromycin), proton pump inhibitors are used to get rid of Helicobacter pylori infection (a bacterial infection of the stomach), which is thought to be one of the main causes of recurring stomach ulcers.

Proton pump inhibitors are also the drugs of first choice for a rare condition called Zollinger-Ellison syndrome. This is a condition where a tumour in the pancreas causes too much stomach acid to be produced and so leads to severe stomach ulceration.



### **Side effects**

The proton pump inhibitors generally don't cause many problems. The most common Side effects are diarrhoea, feeling or being sick, constipation, wind, abdominal pain and headaches. Very rarely they can also cause allergic reactions, itching, dizziness, swollen ankles, muscle and joint pain, blurred vision, depression and a dry mouth. A problem that can occur with long-term use of proton pump inhibitors is stomach infections. Stomach acid helps to kill microscopic organisms (microbes) such as bacteria in the stomach. Because proton pump inhibitors completely stop acid production using them can lead to a growth of microbes in the stomach.



### **Use proton pump inhibitors with care if ...**

You should use a proton pump inhibitor with care if you:

- have liver or kidney problems
- are pregnant or breastfeeding



### **Interactions with other medicines**

Do not take any other medicines or herbal remedies with a proton pump inhibitor, including those you have bought without a prescription, before talking to your doctor or pharmacist.

- The effects of phenytoin (an epilepsy medicine) and warfarin (for preventing blood clots) are increased by some of the proton pump inhibitors.
- The absorption of the antifungal drugs ketoconazole and itraconazole are reduced by proton pump inhibitors.
- The breakdown of diazepam (Valium) in the body may be blocked by some of the proton pump inhibitors so that there is an increased effect of diazepam.



### **How to use a proton pump inhibitor**

The proton pump inhibitors are only available on prescription. They come as tablets, capsules, powder to be made into a suspension, and injections. They are usually taken for 1-2 months but may need to be taken for longer. Once you stop taking a proton pump inhibitor, your

symptoms might come back. If you vomit blood, notice something that looks like coffee grounds in your vomit or pass black tarry stools, see your doctor immediately, as these are signs of intestinal bleeding.



### Common proton pump inhibitors

(The black triangle symbol indicates drugs that are new to the market. This is intended to remind doctors and pharmacists to be particularly vigilant about side effects associated with taking these medicines. At present, the black triangle does not appear on information for patients.)

Proton pump inhibitors

Omeprazole (Losec)

▼ Esomeprazole (Nexium)

Lansoprazole (Zoton)

Pantoprazole (Protium)

Rabeprazole sodium (Pariet)



### Self-help for ulcers

To help heal your ulcer, avoid alcohol, stop smoking and try not to eat or drink things that you know cause your problems such as spicy or fatty foods and coffee. Eat regularly and avoid large meals, and don't take medicines known to irritate the stomach lining such as aspirin or ibuprofen unless your doctor has prescribed them.

August 2001

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